Amendments in the Specification

Applicant respectfully requests that the amendments to the specification as indicated in the reply dated July 1, 2002 (copy enclosed) NOT be entered.

Please amend the paragraph on page 3, lines 7 to 21, to recite:

Previously, as disclosed and claimed in WO 98/51325, which is hereby incorporated by reference in its entirety, we have identified random peptides and their fragments, motifs, derivatives, analogs or peptidomimetics thereof which are capable of specific binding to GIT transport receptors such as the D2H (human D2 clone), hSI (human sucrase isomaltose), HPT1 (human intestinal oligopeptide transporter) and hPEPT1 (human oligopeptide transporter) receptors (hereinafter "GIT targeting agents"). These GIT targeting agents are capable of facilitating transport of an active agent through a human or animal gastro-intestinal tissue and have use, for example, in facilitating transport of active agents from the lumenal side of the GIT into the systemic blood system and/or in targeting active agents to the GIT. Thus, for example, by binding (covalently or noncovalently) the GIT targeting agent to an orally administered active agent, the active agent can be targeted to specific receptor sites or transport pathways which are known to operate in the human gastrointestinal tract, thus facilitating its absorption into the systemic system. Preferably, the active agent is a drug or a drug-containing nano- or microparticle.

Amendments to the Specification:

Please **replace** Table 1, page 19 with the following Table 1

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SEQ ID NO:	Name	Description	Sequence
1	SEQ ID NO:1	PAX2 15 mer fragment-D form retroinversion	rtrlrrnhsshkant
2	SEQ ID NO:2	P31 16 mer fragment- D form retroinversion	gphrrgrpnsrsskrt
3	SEQ ID NO:3	HAX42 14 mer fragment- D form retroinversion	gtsngngccnydgp
4	SEQ ID NO:4	PAX2 15 mer fragment	TNAKHSSHNRRLRTR
5	SEQ ID NO:5	P31 16 mer fragment	TRKSSRSNPRGRRHPG
6	SEQ ID NO:6	HAX42 14 mer fragment	PGDYNCCGNGNSTG
9	ZElan144	dansylated PAX2 15 mer fragment-D form retroinversion	K(dns)-rtrlrrnhsshkant
10	ZElan145	dansylated P31 16 mer fragment- D form retroinversion	K(dns)-gphrrgrpnsrsskrt
11	ZElan146	dansylated HAX42 14 mer fragment- D form retroinversion	K(dns)-gtsngngccnydgp
12	ZElan129	dansylated PAX2 15 mer fragment	K(dns)-TNAKHSSHNRRLRTR
13	ZElan031	dansylated P31 16 mer fragment	K(dns)-TRKSSRSNPRGRRHPG
14	ZElan091	dansylated HAX42 14 mer fragment	K(dns)-PGDYNCCGNGNSTG

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Please **replace** Table 3, page 21 with the following Table 3:

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Name	**Sequence**	**K_D (μmol)**
ZElan018	K(dns)-STPPSREAYSRPYSVDSDSDTNAKHSSHNRRLRTRSRPNG (SEQ ID NO:7)	>50.0
ZElan129	K(dns)-TNAKHSSHNRRLRTR (SEQ ID NO:12)	29.6
ZElan144	K(dns)-rtrlrrnhsshkant (SEQ ID NO:9)	28.8
ZElan021	K(dns)-SDHALGTNLRSDNAKEPGDYNCCGNGNSTGRKVFNRRRPSAIPT (SEQ ID NO:8)	6.7
ZElan091	K(dns)-PGDYNCCGNGNSTG (SEQ ID NO:14)	0.75
ZElan146	K(dns)-gtsngngccnydgp (SEQ ID NO:11)	21.65

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Please **replace** the paragraph at page 20, line 22 to page 21, line 2, already amended on October 5, 2001, with the following paragraph:

-- ZElan021, full length HAX42 [K(dns)-SDHALGTNLRSDNAKEPGDYNCCGNGNSTGRKVFNRRRPSAIPT] (SEQ ID NO:53; dansylated version is SEQ ID NO:8) was given the arbitrary value of 1.00 for binding to P100 at a given peptide concentration determined from the signal-to-noise ratio data. Table 2 shows the results of P100 assays with the HAX42 related peptides ZElan021, Zelan091 and ZElan146. Assay number 1 was at 20 μg/ml; 2 and 3 were at 50 μg/ml; and 4 through 8 were at 25 μg/ml. The results for the retro-inverted form, Zelan 146 show reasonable binding compared to the HAX42 fragment Zelan091 and that the activity of the GIT targeting agent was not eliminated when converted to its retro-inverted form. --

Please **replace** the paragraph at page 21, lines 5-11, already amended on October 5, 2001, with the following paragraph:

--K_D values, or the concentration of the peptide required to reach half maximal binding to Caco-2 P100 fractions, are given in Table 3 for ZElan021, full length HAX42, [K(dns)-SDHALGTNLRSDNAKEPGDYNCCGNGNSTGRKVFNRRRPSAIPT] (SEQ ID NO:53; dansylated version is SEQ ID NO:8), HAX42 fragment ZElan091, and the retro-inverted form of this fragment, ZElan146 as well as for ZElan018, full length PAX2, [K(dns)-STPPSREAYSRPYSVDS DSDTNAKHSSHNRRLRTRSRPNG] (SEQ ID NO:7; dansylated version is SEQ ID NO:15), PAX2 fragment ZElan129, and the retro-inverted form of this fragment, ZELan144.--

On page 5, after line 12, please **insert** the following paragraphs:

-- The HPT1, hPEPT1, D2H, and hSI receptors were selected for cloning as GIT receptor targets based on several criteria, including: (1) expression on surface of epithelial cells in gastro-intestinal tract (GIT); (2) expression along the length of small intestine (HPT1, hPEPT1, D2H); (3) expression locally at high concentration (hSI); (4) large putative extracellular domains facing into the lumen of the GIT; and (5) extracellular domains that permit easy access and bioadhesion by targeting particles.

The four recombinant receptor sites screened with the peptide libraries additionally have the following characteristics:

Receptor	Characteristics
D2H	Transport of neutral/basic amino acids; a transport activating protein for a range of amino acid translocases
hS1	Metabolism of sucrose and other sugars, represents 9% of brush border membrane protein Jejunum
HPT1	di/tri peptide transporter or facilitator of peptide transport
hPEPT1	di/tri peptide transporter

6.2. Cloning of Extracellular Domain of Selected Receptor Site

The following receptor domains were cloned and expressed as His-tag fusion proteins by standard techniques:

Receptor	Domain (amino acid residues)
hPEPT1[a]	391-571
HPT1[b]	29-273
hSI[c]	272-667
D2H[d]	387-685

[a] Liang et al., 1995, J. Biol. Chern. 270: 6456-6463;
[b] Dantzig et al., 1994, Association of Intestinal Peptide Transport with a Protein Related to the Cadherin Superfamily;

[c] Chantret et al., Biochem. J. 285: 915-923;
[d] Bertran et al., J. Biol. Chem. 268: 14842-14949.

The receptor proteins were expressed as His-tag fusion proteins and affinity purified under denaturing conditions, using urea or guanidine HCl, utilizing the pET His-tag metal chelate affinity for Ni-NTA Agarose (Hochuli, E., Purification of recombinant proteins with metal chelate adsorbent, Genetic Engineering, Principals and Methods (J.K. Setlow, ed.), Plenum Press, NY, Vol. 12 (1990), pp. 87-98).

As indicated in WO 98/51325, phage which showed specificity to a GIT receptor was further characterized by ELISA on a variety of recombinant proteins. Phage which continued to exhibit GIT receptor specificity was sequenced. Their insert sequences are summarized as follows:

hSI	SEQ. ID.NO	TARGET BINDING PHAGE INSERT SEQUENCE
S15	16.	RSGAYESPDGRGGRSYVGGGGGCGNIGRKHNLWGLRTASPACWD
S21	17.	SPRSFWPVVSRHESFGISNYLGCGYRTCISGTMTKSSPIYPRHS
S22	18.	SSSSDWGGVPGKVVRERFKGRGCGISITSVLTGKPNPCPEPKAA
Sni10	19.	RVGQCTDSDVRRPWARSCAHQGCGAGTRNSHGCITRPLRQASAH
Sni28	20.	SHSGGMNRAYGDVFRELRDRWNATSHHTRPTPQLPRGPN
Sni34	21.	SPCGGSWGRFMQGGLFGGRTDGCGAHRNRTSASLEPPSSDY
Sni38	22.	RGAADQRRGWSENLGLPRVGWDAIAHNSYTFTSRRPRPP
Sni45	23.	SGGEVSSWGRVNDLCARVSWTGCGTARSARTDNKGFLPKHSSLR
SniAX2	24.	SDSDGDHYGLRGGVRCSLRDRGCGLALSTVHAGPPSFYPKLSSP
SniAX4	25.	RSLGNYGVTGTVDVTVLPMPGHANHLGVSSASSSDPPRR
SniAX6	26.	RTTTAKGCLLGSFGVLSGCSFTPTSPPPHLGYPPHSVN
SniAX8	27.	SPKLSSVGVMTKVTELPTEGPNAISIPISATLGPRNPLR

D2H

DAB3	28.	RWCGAELCNSVTKKFRPGWRDHANPSTHHRTPPPSQSSP
DAB7	29	RWCGADDPCGASRWRGGNSLFGCGLRCSAAQSTPSGRIHSTSTS
DAB10	30.	SKSGEGGDSSRGETGWARVRSHAMTAGRFRWYNQLPSDR
DAB18	31.	RSSANNCEWKSDWMRRACIARYANSSGPARAVDTKAAP
DAB24	32.	SKWSWSSRWGSPQDKVEKTRAGCGGSPSSTNCHPYTFAPPPQAG
DAB30	33.	SGFWEFSRGLWDGENRKSVRSGCGFRGSSAQGPCPVTPATIDKH
DAX15	34.	SESGRCRSVSRWMTTWQTQKGGCGSNVSRGSPLDPSHQTGHATT
DAX23	35.	REWRFAGPPLDLWAGPSLPSFNASSHPRALRTYWSQRPR
DAX24	36.	RMEDIKNSGWRDSCRWGDLRPGCGSRQWYPSNMRSSRDYPAGGH
DAX27	37.	SHPWYRHWNHGDFSGSGQSRHTPPESPHPGRPNATI
DCX8	38.	RYKHDIGCDAGVDKKSSSVRGGCGAHSSPPRAGRGPRGTMVSRL
DCX11	39.	SQGSKQCMQYRTGRLTVGSEYGCGMNPARHATPAYPARLLPRYR
DCX26	40.	SGRTTSEISGLWGWGDDRS GYGWGNTLRPNYIPYRQATNRHRYT
DCX33	41.	RWNWTVLPATGGHYWTRSTDYHAINNHRPSIPHQHPTPI
DCX36	42.	SWSSWNWSSKTTRLGDRATREGCGPSQSDGCPYNGRLTTVKPRT
DCX39	43.	SGSLNAWQPRSWVGGAFRSHANNNLNPKPTMVTRHPT
DCX42	44.	RYSGLSPRDNGPACSQEATLEGCGAQRLMSTRRKGRNSRPGWTL
DCX45	45.	SVGNDKTSRPVSFYGRVSDLWNASLMPKRTPSSKRHDDG

hPEPT1

PAX9	46.	RWPSVGYKGNGSDTIDVHSNDASTKRSLIYNHRRPLFP
PAX14	47.	RTFENDGLGVGRSIQKKSDRWYASHNIRSHFASMSPAGK
PAX15	48.	SYCRVKGGGEGGHTDSNLARSGCGKVARTSRLQHINPRATPPSR
PAX16	49.	SWTRWGKHTHGGFVNKSPPGKNATSPYTDAQLPSDQGPP

PAX17	50.	SQVDSFRNSFRWYEPSRALCHGCGKRDTSTTRIHNSPSDSYPTR
PAX18	51.	SFLRFQSPRFEDYSRTISRLRNATNPSNVSDAHNNRALA
PAX35	52.	RSITDGGINEVDLSSVSNVLENANSHRAYRKHRPTLKRP
PAX38	53.	SSKVSSPRDPTVPRKGGNVDYGCGHRSSARMPTSALSSITKCYT
PAX40	54.	RASTQGGRGVAPEFGASVLGRGCGSATYYTNSTSCKDAMGHNYS
PAX43	55.	RWCEKHKFTAARCSAGAGFERDASRPPQPAHRDNTNRNA
PAX45	56.	SFQVYPDHGLERHALDGTGPLYAMPGRWIRARPQNRDRQ
PAX46	57.	SRCTDNEQCPDTGTRSRSVSNARYFSSRLLKTHAPHRP
P31	58.	SARDSGPAEDGSRAVRLNGVENANTRKSSRSNPRGRRHP
P90	59.	SSADAEKCAGSLLWWGRQNNSGCGSPTKKHLKHRNRSQTSSSSH
5PAX3	60.	RPKNVADAYSSQDGAAAEETSHASNAARKSPKHKPLRRP
5PAX5	61.	RGSTGTAGGERSGVLNLHTRDNASGSGFKPWYPSNRGHK
5PAX7	62.	RWGWERSPSDYDSDMDLGARRYATRTHRAPPRVLKAPLP
5PAX12	63.	RGWKCEGSQAAYGDKDIGRSRGCGSITKNNTNHAHPSHGAVAKI

HPT-1

HAX9	64.	SREEANWDGYKREMSHRSRFWDATHLSRPRRPANSGDPN
HAX35	65.	EWYSWKRSSKSTGLGDTATREGCGPSQSDGCPYNGRLTTVKPRK
HAX40	66.	REFAERRLWGCDDLSWRLDAEGCGPTPSNRAVKHRKPRPRSPAL
HAX42	67.	SDHALGTNLRSDNAKEPGDYNCCGNGNSTGRKVFNRRRPSAIPT
HCA3	68.	RHISEYSFANSHLMGGESKRKGCGINGSFSPTCPRSPTPAFRRT
H40	69.	SRESGMWGSWWRGHRLNSTGGNANMNASLPPDPPVSTP
PAX2	70.	STPPSREAYSRPYSVDSDSDTNAKHSSHNRRLRTRSRPN

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On page 6, after line 14, please **insert** the following paragraph:

--In a specific embodiment of the invention, proteins consisting of or, alternatively, comprising all or a fragment of a GIT transport receptor-binding peptide consisting of at least 5, 10, 15, 20, 25, 30 or 35 (contiguous) amino acids of the full-length GIT transport receptor-binding peptide are provided. In a specific embodiment, such proteins are not more than 20, 30, 40, 50, or 75 amino acids in length. Derivatives or analogs of GIT transport receptor-binding peptides include but are not limited to those molecules comprising regions that are substantially homologous to GIT transport receptor-binding peptides or fragments thereof (e.g., at least 50%, 60%, 70%, 80% or 90% identity) (e.g., over an identical size sequence or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art) or whose encoding nucleic acid is capable of hybridizing to a coding GIT transport receptor-binding peptide sequence, under stringent, moderately stringent, or nonstringent conditions. --

To see how changes were made in Tables 1 and 3 and replaced paragraphs, please go to Amendments with Markings Showing Changes on Page 32.